4164-01-P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA-2016-D-0643]

Labeling for Biosimilar and Interchangeable Biosimilar Products; Draft Guidance for Industry; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice of availability.

SUMMARY: The Food and Drug Administration (FDA or Agency) is announcing the availability of a draft guidance for industry entitled "Labeling for Biosimilar and Interchangeable Biosimilar Products." This draft guidance is intended to help applicants develop draft labeling for proposed biosimilar and interchangeable biosimilar products. The recommendations for biosimilar and interchangeable biosimilar product labeling in this draft guidance pertain only to the prescribing information, except for certain recommendations pertaining to FDA-approved patient labeling (e.g., Patient Information, Medication Guide, Instructions for Use). This draft guidance provides an overview of FDA's recommendations for labeling for biosimilar and interchangeable biosimilar products. When finalized, this draft guidance will revise and replace the guidance for industry entitled "Labeling for Biosimilar Products."

DATES: Submit either electronic or written comments on the draft guidance by [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*] to ensure that the Agency considers your comment on this draft guidance before it begins work on the final version of the guidance.

ADDRESSES: You may submit comments on any guidance at any time as follows:

Electronic Submissions

Submit electronic comments in the following way:

- Federal eRulemaking Portal: https://www.regulations.gov. Follow the instructions for submitting comments. Comments submitted electronically, including attachments, to https://www.regulations.gov will be posted to the docket unchanged. Because your comment will be made public, you are solely responsible for ensuring that your comment does not include any confidential information that you or a third party may not wish to be posted, such as medical information, your or anyone else's Social Security number, or confidential business information, such as a manufacturing process. Please note that if you include your name, contact information, or other information that identifies you in the body of your comments, that information will be posted on https://www.regulations.gov.
- If you want to submit a comment with confidential information that you do not wish to be made available to the public, submit the comment as a written/paper submission and in the manner detailed (see "Written/Paper Submissions" and "Instructions").

Written/Paper Submissions

Submit written/paper submissions as follows:

- Mail/Hand delivery/Courier (for written/paper submissions): Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852.
- For written/paper comments submitted to the Dockets Management Staff, FDA will post your comment, as well as any attachments, except for information submitted, marked and identified, as confidential, if submitted as detailed in "Instructions."

Instructions: All submissions received must include the Docket No. FDA-2016-D-0643 for "Labeling for Biosimilar and Interchangeable Biosimilar Products." Received comments will be placed in the docket and, except for those submitted as "Confidential Submissions," publicly viewable at https://www.regulations.gov or at the Dockets Management Staff between 9 a.m. and 4 p.m., Monday through Friday, 240-402-7500.

- Confidential Submissions--To submit a comment with confidential information that you do not wish to be made publicly available, submit your comments only as a written/paper submission. You should submit two copies total. One copy will include the information you claim to be confidential with a heading or cover note that states "THIS DOCUMENT CONTAINS CONFIDENTIAL INFORMATION." The Agency will review this copy, including the claimed confidential information, in its consideration of comments. The second copy, which will have the claimed confidential information redacted/blacked out, will be available for public viewing and posted on https://www.regulations.gov. Submit both copies to the Dockets Management Staff. If you do not wish your name and contact information to be made publicly available, you can provide this information on the cover sheet and not in the body of your comments and you must identify this information as "confidential." Any information marked as "confidential" will not be disclosed except in accordance with 21 CFR 10.20 and other applicable disclosure law. For more information about FDA's posting of comments to public dockets, see 80 FR 56469, September 18, 2015, or access the information at: https://www.govinfo.gov/content/pkg/FR-2015-09-18/pdf/2015-23389.pdf.

Docket: For access to the docket to read background documents or the electronic and written/paper comments received, go to https://www.regulations.gov and insert the docket number, found in brackets in the heading of this document, into the "Search" box and follow the prompts and/or go to the Dockets Management Staff, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852, 240-402-7500.

You may submit comments on any guidance at any time (see 21 CFR 10.115(g)(5)).

Submit written requests for single copies of the draft guidance to the Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10001 New Hampshire Ave., Hillandale Building, 4th Floor, Silver Spring, MD 20993-0002; or the Office of Communication, Outreach and Development, Center for Biologics Evaluation and

Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002. Send one self-addressed adhesive label to assist that office in processing your requests. See the SUPPLEMENTARY INFORMATION section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Sandra Benton, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 22, Rm. 1132, Silver Spring, MD 20993, 301-796-1042, Sandra.Benton@fda.hhs.gov; or Anne Taylor, Center for Biologics Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 71, Rm. 7301, Silver Spring, MD 20993-0002, 240-402-7911.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry entitled "Labeling for Biosimilar and Interchangeable Biosimilar Products." Section 351(k) of the Public Health Service Act (PHS Act) (42 U.S.C. 262(k)) provides an abbreviated licensure pathway for biological products shown to be biosimilar to, or interchangeable with, an FDA-licensed reference product. Section 351(k) of the PHS Act sets forth the requirements for an application for a proposed biosimilar product and an application or a supplement for a proposed interchangeable biosimilar product. Under section 351(k) of the PHS Act, a proposed biological product that is demonstrated to be biosimilar to, or interchangeable with, a reference product can rely on certain existing scientific knowledge about the safety, purity, and potency of the reference product to support licensure, and this is reflected in the approach to biosimilar and interchangeable biosimilar product labeling.

In this draft guidance, FDA outlines its recommendations for biosimilar and interchangeable biosimilar product labeling. A demonstration of biosimilarity or interchangeability means, among other things, that FDA has determined that there are no clinically meaningful differences between the proposed product and the reference product in

terms of safety, purity, and potency. Accordingly, the draft guidance includes a recommendation that biosimilar and interchangeable biosimilar product applicants should incorporate relevant data and information from the reference product labeling, with appropriate modifications.

When finalized, this draft guidance will revise and replace the guidance for industry entitled "Labeling for Biosimilar Products" (available at https://www.fda.gov/media/96894/download) issued July 19, 2018 (83 FR 34141). Significant changes from the final to this draft include recommendations on the following topics:

- Labeling for interchangeable biosimilar products;
- Product identification when the reference product labeling describes a clinical study conducted with a non-U.S.-approved biological product;
- Pediatric use statements; and
- Incorporating relevant immunogenicity data and information from the reference product labeling in the biosimilar or interchangeable biosimilar product labeling.

This draft guidance also addresses topics previously addressed in Q.I.27 and Q.I.28 of the draft guidance "Biosimilarity and Interchangeability: Additional Draft Q&As on Biosimilar Development and the BPCI Act" issued on November 19, 2020 (Additional Draft Q&As guidance). FDA considered comments it received regarding these Q&As when preparing this draft guidance. The Additional Draft Q&As guidance has been revised to remove Q.I.27 and Q.I.28, with the remaining Q&As unchanged. The remaining Q&As can be found in the draft guidance "Biosimilarity and Interchangeability: Additional Draft Q&As on Biosimilar Development and the BPCI Act (Revision 1)."

Eight years have passed since FDA approved the first biosimilar product. In this time, FDA has approved over 40 biosimilar products, including multiple interchangeable biosimilar products, and has gained valuable experience about labeling considerations for biosimilar and interchangeable biosimilar products, including labeling statements in the Highlights of the Prescribing Information that explain biosimilarity and interchangeability. First, it has become

clear that an applicant may choose to submit a single 351(k) biologics license application (BLA) seeking to license both biosimilar and interchangeable biosimilar products. Draft labeling for such applications would need to address both biosimilar and interchangeable biosimilar products, and the status of a particular product within such a BLA can change over time, for example, as relevant exclusivities expire. Determining how to appropriately label such products and keep labeling up to date without causing undue confusion has proven challenging. Moreover, a labeling statement noting that certain products within a 351(k) BLA have been approved as interchangeable, and explaining the interchangeability standard, is not likely to be useful to prescribers, who can prescribe both biosimilar and interchangeable biosimilar products in place of the reference product with equal confidence that they are as safe and effective as their reference products. Additionally, FDA's Purple Book Database of Licensed Biological Products (the Purple Book) (available at https://purplebooksearch.fda.gov) has evolved as a resource for patients, pharmacists, physicians, and other health care providers to easily identify approved biosimilar and interchangeable biosimilar products. Because the Purple Book is available as an easy-to-use resource for pharmacists, and interchangeability, as defined in section 351(i)(3) of the PHS Act, pertains to substitution of an interchangeable biosimilar product for its reference product "without the intervention of the [prescribing] health care provider" (i.e., pharmacy-level substitution), information about interchangeability is more appropriately located in the Purple Book rather than labeling. Consistent with this evolution in our thinking, the draft guidance states that both biosimilar and interchangeable biosimilar products should contain the same biosimilarity statement in the Highlights of the Prescribing Information. This statement is applicable to biosimilar and interchangeable biosimilar products. Accordingly, as described above, FDA has withdrawn the Q&As in its Additional Draft Q&As guidance regarding inclusion of an interchangeability statement in the labeling of products licensed as interchangeable.

Finally, we invite comment on biosimilarity statements, such as a statement described in section IV.C.1.b of the draft guidance, in the Highlights of the Prescribing Information. Specifically, FDA invites comment on how useful such biosimilarity statements have been for healthcare practitioners and the public, whether such statements can be improved to provide more clarity on what biosimilarity means, and whether biosimilar and interchangeable biosimilar product labeling should include such a statement at all.

This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the current thinking of FDA on "Labeling for Biosimilar and Interchangeable Biosimilar Products." It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations.

II. Paperwork Reduction Act of 1995

While this guidance contains no collection of information, it does refer to previously approved FDA collections of information. Therefore, clearance by the Office of Management and Budget (OMB) under the Paperwork Reduction Act of 1995 (PRA) (44 U.S.C. 3501-3521) is not required for this guidance. The previously approved collections of information are subject to review by OMB under the PRA. The collections of information for the submission of a BLA under section 351(k) of the PHS Act have been approved under OMB control number 0910-0718; the collections of information in 21 CFR 201.56 and 201.57 for the submission of labeling have been approved under OMB control number 0910-0572; the collections of information in 21 CFR part 208 for Medication Guides have been approved under OMB control number 0910-0393; the collections of information in 21 CFR 312.47 for meetings with FDA have been approved under OMB control number 0910-0014; the collections of information in 21 CFR part 600 for the submission of adverse experience reporting for licensed biological products and general records have been approved under OMB control number 0910-0308; and the collections

of information in 21 CFR part 601 for the submission of labeling in a BLA or supplement to a BLA have been approved under OMB control number 0910-0338.

III. Electronic Access

Persons with access to the internet may obtain the draft guidance at https://www.fda.gov/drugs/guidance-compliance-regulatory-information/guidances-drugs, https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances, https://www.fda.gov/regulatory-information/search-fda-guidance-documents, or https://www.regulations.gov.

Dated: September 13, 2023.

Lauren K. Roth,

Associate Commissioner for Policy.

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